

### REMARKS

Claims 1 to 12 have been presented for examination and claims 13 to 26 are now in the application. No additional fee is required.

The Examiner indicates that claims 1 to 12 are drawn to compositions and methods for topically treating various conditions, including inflammatory conditions as well as psoriasis. The Examiner requires that Applicants elect a specific medical condition disclosed for examination on the merits. In accordance with the requirements of 37 CFR 1.146, Applicants elect the method of treating Lupus erythematosus of original claim 12 and new claim 13 for further prosecution. New claims 14 to 26 read on the elected invention.

Claims 1 to 12, now 13 to 26, are rejected under 35 USC 103 over the Okuhara, et al. European Patent application 184,162 (of record). The Examiner indicates that Okuhara discloses pharmaceutical compositions containing the compounds of the present invention for use in treating Lupus erythematosus by external administration. The Examiner argues that this would motivate one skilled in the art to prepare compositions containing the prior art compounds for treating Lupus erythematosus topically. Applicants respectfully disagree and traverse the rejection.

As discussed on pages 2 and 3 of the instant specification, the topical efficacy of the claimed compounds is totally unexpected in light of the results found with the known immunosuppressant cyclosporine. There is nothing in Okuhara which would even vaguely suggest that, unlike the prior art immunosuppressant, the present compounds would exhibit surprising topical activity; and there is certainly nothing which would motivate one skilled in the art to investigate such activity. It will be noted that in none of the testing carried out in the Okuhara application is the compound administered topically. It will also be noted that the fungi used in the antimicrobial test 2, *Aspergillus fumigatus* and *Fusarium oxysporum*, are organisms which are treated systemically. No testing was carried out with any organisms, such as dermatophytes or yeast fungus, which would show topical efficacy. All of the activities disclosed in the reference, including Lupus erythematosus, require systemic treatment. The external administration contemplated by Okuhara clearly involves those modes of administration, such as nasal, buccal, rectal, etc., which would produce a systemic effect. Topical administration certainly would not be an obvious alternative for the systemic treatment of the conditions of the reference. As indicated above, the known immunosuppressant, cyclosporine, has little activity in the topical treatment of psoriasis. One skilled in the art would certainly consider it unexpected if a cyclic immunosuppressant with similar activities were found to have effective topical activity. Applicants submit that there is nothing in the Okuhara application, which would lead one to expect that the condition disclosed could be effectively

treated topically with the claimed compounds. Okuhara does not disclose a use for a topical pharmaceutical composition and, therefore, would not render such a composition or its use in treating Lupus erythematosus obvious. In order to distinguish more clearly over the Okuhara use and compositions, however, Applicants have limited the method claims to the treatment of the cutaneous manifestations of Lupus erythematosus, and the composition claims to the lotion, gels, and creams of original claims 7 and 8. This method and these compositions are clearly not suggested by the Okuhara disclosure. Applicants, therefore, believe that the presently claimed topical composition and method of treating the cutaneous manifestations of Lupus erythematosus are patentable over the Okuhara, et al. application; and accordingly, it is respectfully requested that the Examiner reconsider the instant rejection under 35 USC 103 and withdraw it.

Claims 5 to 8 and presumably new claims 19 to 26 are rejected over the claims of U.S. Patent No. 5,366,971. The Examiner indicates that the compositions of the rejected claims were examined with the elected invention in the parent case, Serial No. 07/982,925, which issued as USP 5,366,971, and now raises questions of double patenting. In accordance with the requirements of Rule 78(d) and Rule 321(b), Applicants will submit a Terminal Disclaimer to disclaim that portion of the term of any patent issuing on the present application extending beyond November 22, 2011, the expiration date of grandparent application Serial No. 07/982,925, filed November 30, 1992, which issued as the

aforementioned United States Patent No. 5,366,971 on November 22, 1994. The disclaimer will also state that any patent issuing on this application shall be enforceable only for and during such period that the ownership of this patent is the same as the ownership of USP 5,366,971.

Claims 1 to 4, 9, and 10 are rejected under the second paragraph of 35 U.S.C. 112. The Examiner indicates that the claims are improper because of the "use of" language in the claims. Applicants have canceled these claims from the present application, and no further comment regarding this rejection is believed necessary.

The basis for new claims 13 to 26 is as follows:

<u>Claims</u>	<u>Basis</u>
13	Original claims 11 and 12;
14 and 20	Page 17, lines 11 to 14;
15 and 21	Page 14, compounds A and B;
16 and 22	Original claim 3;
17 and 23	Original claim 4;
18	Original claims 7 and 8;
19	Original claims 5, 7, and 8; and
24, 25, and 26	Original claim 8.

The new claims are fully supported by the present application; and therefore, it is respectfully requested that they be entered.

Enclosed in accordance with 37 CFR 1.97 and 1.98 is a completed Form PTO-1440, which lists all of the relevant art known to Applicants. A copy of the first 80 documents listed was submitted with the Information Disclosure Statement filed May 10, 1993 on parent application Serial No. 07/982,925; and copies of these citations are not enclosed. In accordance with 37 CFR 1.98(a)(2), a copy of the additional Cole, et al art cited is enclosed with this amendment. The Cole publication, which is not a reference against the present application, indicates that with cyclosporine, only one patient in ten with allergic contact dermatitis showed improvement. The presently claimed invention is clearly patentable over this art, and no further comment regarding it is deemed necessary.

The Claim of Priority and the filing of the priority documents indicated on page 5 of the filing papers has not as yet been acknowledged by the Examiner.

It is respectfully requested that the period for filing a response to the Office Action of October 25, 1995 on the above-identified application Serial No. 08/471,146 originally set to expire January 25 1996 be extended for three months until April 22 1996.

Please charge the Information Disclosure Statement fee of \$220.00 required by 37 CFR 1.17(p) and the extension fee of \$900.00 required by 37 CFR 1.17(c) to Deposit Account No. 19-0134 in the name of Sandoz Corporation.

In view of the above amendments and comments, it is believed that the instant application is now in condition for allowance; and accordingly, it is respectfully requested that the Examiner withdraw the rejection of the present claims and pass the application to issue.

Respectfully submitted,

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April 25, 1996

Enclosures: Duplicate copies of page 11 of this Amendment;  
Form PTO-1449 plus citation (1);  
COM Stamp; Postcard.